The Claims

1.   (Currently Amended) An apparatus comprising:

one or more processors; and

a memory coupled to the processors comprising one or more instructions, the processors operable when executing the instructions to:

determine an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

generate a first set and at least a second set of empirically derived parameters, each set including a minimum binding-energy distance value and a well-depth value of the atom-pair type;

calculate a first and second repulsion term of the protein-ligand atom pair according to the first and second sets of empirically derived minimum binding-energy distance and well-depth values, respectively a minimum binding-energy distance value and a well-depth value of the atom-pair type;

calculate a first and second potential of mean force (PMF) of the protein-ligand atom pair according to the calculated first and second repulsion terms, respectively, term of the protein-ligand atom pair;

calculate a first and second PMF score of the protein-ligand complex according to the calculated first and second PMF of the protein-ligand atom pair, respectively, each the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex;

predict first and second structures of the protein-ligand complex according to the first and second PMF scores, respectively;

calculate a first root mean square (RMS) deviation between the first predicted structure and an actual, analyzed structure of the protein-ligand complex;

calculate a second root mean square (RMS) deviation between the second predicted structure and the actual, analyzed structure of the protein-ligand complex;

determine agreement between the first set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the first RMS deviation;

determine agreement between the second set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the second RMS deviation; and

communicate at least the PMF score from the first and second PMF scores that is in best agreement with the actual, analyzed protein-ligand atom pair in a user readable format for presentation to a user.

2-8   (Canceled)

9.   (Currently Amended) The apparatus of Claim 5, Claim 1, wherein one or more of the first set of empirically derived minimum binding-energy distance distances and well-depth values or second sets of empirically derived minimum binding-energy distance distances and well-depth values are each a product of one or more manual processes or automatic processes.

10.   (Previously Presented)   The apparatus of Claim 9, wherein at least one of the automatic processes comprises execution of a genetic algorithm.

11.   (Currently Amended) A method comprising:

determining an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

generating a first set and at least a second set of empirically derived parameters, each set including a minimum binding-energy distance value and a well-depth value of the atom-pair type;

calculating a first and second repulsion term of the protein-ligand atom pair according to the first and second sets of empirically derived minimum binding-energy distance and well-depth values, respectively a minimum binding energy distance value and a well depth value of the atom pair type;

calculating a first and second potential of mean force (PMF) of the protein-ligand atom pair according to the calculated first and second repulsion terms, respectively term of the protein-ligand atom pair;

calculating a <u>first and second</u> PMF score of the protein-ligand complex according to the calculated <u>first and second</u> PMF of the protein-ligand atom pair, <u>respectively, each</u> ~~the~~ PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex;

<u>predicting first and second structures of the protein-ligand complex according to the first and second PMF scores, respectively;</u>

<u>calculating a first root mean square (RMS) deviation between the first predicted structure and an actual, analyzed structure of the protein-ligand complex;</u>

<u>calculating a second root mean square (RMS) deviation between the second predicted structure and the actual, analyzed structure of the protein-ligand complex;</u>

<u>determining agreement between the first set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the first RMS deviation;</u>

<u>determining agreement between the second set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the second RMS deviation; and</u>

communicating <u>at least</u> the PMF score <u>from the first and second PMF scores that is in best agreement with the actual, analyzed protein-ligand atom pair in a user readable format</u> ~~for presentation to a user~~.

12-18   (Canceled)

19.   (Currently Amended) The method of ~~Claim 15,~~ <u>Claim 11,</u> wherein one or more of the first set of empirically derived minimum binding-energy <u>distance</u> ~~distances~~ and well-depth values or second sets of empirically derived minimum binding-energy <u>distance</u> ~~distances~~ and well-depth values are each a product of one or more manual processes or automatic processes.

20.   (Previously Presented)   The method of Claim 19, wherein at least one of the automatic processes comprises execution of a genetic algorithm.

21.   (Currently Amended) Software encoded in one or more computer-readable tangible media and when executed operable to:

determine an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

generate a first set and at least a second set of empirically derived parameters, each set including a minimum binding-energy distance value and a well-depth value of the atom-pair type;

calculate a first and second repulsion term of the protein-ligand atom pair according to the first and second sets of empirically derived minimum binding-energy distance and well-depth values, respectively a minimum binding energy distance value and a well depth value of the atom-pair type;

calculate a first and second potential of mean force (PMF) of the protein-ligand atom pair according to the calculated first and second repulsion terms, respectively, term of the protein-ligand atom pair;

calculate a first and second PMF score of the protein-ligand complex according to the calculated first and second PMF of the protein-ligand atom pair, respectively, each the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex;

predict first and second structures of the protein-ligand complex according to the first and second PMF scores, respectively;

calculate a first root mean square (RMS) deviation between the first predicted structure and an actual, analyzed structure of the protein-ligand complex;

calculate a second root mean square (RMS) deviation between the second predicted structure and the actual, analyzed structure of the protein-ligand complex;

determine agreement between the first set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the first RMS deviation;

determine agreement between the second set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the second RMS deviation; and

communicate <u>at least</u> the PMF score <u>from the first and second PMF scores that is in best agreement with the actual, analyzed protein-ligand atom pair in a user readable format</u> ~~for presentation to a user~~.

22-28   (Canceled)

29.   (Currently Amended) The software of ~~Claim 21,~~ <u>Claim 25,</u> wherein one or more of the first set of empirically derived minimum binding-energy <u>distance</u> ~~distances~~ and well-depth values or second sets of empirically derived minimum binding-energy <u>distance</u> ~~distances~~ and well-depth values are each a product of one or more manual processes or automatic processes.

30.   (Previously Presented)   The software of Claim 29, wherein at least one of the automatic processes comprises execution of a genetic algorithm.

31.   (Currently Amended) A system comprising:

means for determining an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

<u>means for generating a first set and at least a second set of empirically derived parameters, each set including a minimum binding-energy distance value and a well-depth value of the atom-pair type;</u>

means for calculating a <u>first and second</u> repulsion term of the protein-ligand atom pair according to <u>the first and second sets of empirically derived minimum binding-energy distance and well-depth values, respectively</u> ~~a minimum binding-energy distance value and a well-depth value of the atom-pair type~~;

means for calculating a <u>first and second</u> potential of mean force (PMF) of the protein-ligand atom pair according to the calculated <u>first and second</u> repulsion <u>terms, respectively</u> ~~term~~ of the protein-ligand atom pair;

means for calculating a <u>first and second</u> PMF score of the protein-ligand complex according to the calculated <u>first and second</u> PMF of the protein-ligand atom pair, <u>respectively,</u>

each ~~the~~ PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex;

means for predicting first and second structures of the protein-ligand complex according to the first and second PMF scores, respectively;

means for calculating a first root mean square (RMS) deviation between the first predicted structure and an actual, analyzed structure of the protein-ligand complex;

means for calculating a second root mean square (RMS) deviation between the second predicted structure and the actual, analyzed structure of the protein-ligand complex;

means for determining agreement between the first set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the first RMS deviation;

means for determining agreement between the second set of empirically derived minimum binding-energy distance and well-depth values and the actual, analyzed protein-ligand atom pair based at least in part on the second RMS deviation; and

means for communicating at least the PMF score from the first and second PMF scores that is in best agreement with the actual, analyzed protein-ligand atom pair in a user readable format ~~for presentation to a user~~.